

Application No. 10/030,350
Responsive to Restriction Requirement of September 16, 2003
Amendment and Response filed March 16, 2004

Listing of Claims.

Claims 1-20 (cancelled).

Claim 21 (previously cancelled).

Claim 22 (currently amended): ~~Process~~ A method for the preparation of cells suitable for transplantation into a mammal, which cells are capable of forming amyloid deposits, said ~~method process~~ comprising contacting the cells *in vitro* with an inhibitor of amyloid deposit formation.

Claim 23 (currently amended): ~~Process~~ The method according to claim 22, wherein said inhibitor causes breakdown of amyloid deposits, the deposits having been formed by said cells prior to said contacting.

Claim 24 (currently amended): ~~Process~~ The method according to claim 22, ~~in which the~~ wherein said cells are cultured in the presence of the inhibitor.

Claim 25 (previously cancelled).

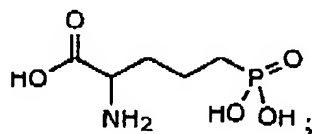
Claim 26 (previously cancelled).

Claim 27 (currently amended): ~~Process~~ The method according to claim 22, wherein ~~the~~ inhibitor is said inhibitor comprises a compound selected from the group consisting of

(i) 3-(3-hydroxy-1-propyl)amino-1-propanesulfonic acid

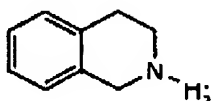


(ii) DL-2-amino-5-phosphovaleric acid

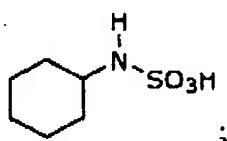


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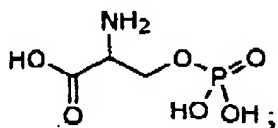
(iii) 1,2,3,4-tetrahydroisoquinoline



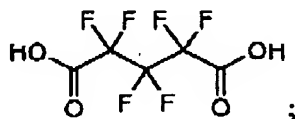
(iv) cyclohexylsulfamic acid



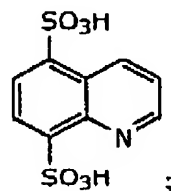
(v) O-phospho-L-serine



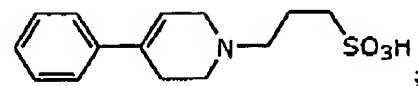
(vi) hexafluoroglutaric acid



(vii) 8-methoxyquinoline-5-sulfonic acid

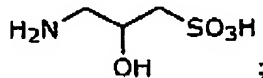


(viii) 4-phenyl-1-(3'-sulfopropyl)-1,2,3,6-tetrahydropyridine



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(ix) 3-amino-2-hydroxy-1-propanesulfonic acid



(x) 3-dimethylamino-1-propanesulfonic acid



and pharmaceutically acceptable esters, acids, and salts or a salt thereof.

Claim 28 (previously cancelled).

Claim 29 (previously cancelled).

Claim 30 (previously cancelled).

Claim 31 (previously cancelled).

Claim 32 (currently amended): A culture medium or a culture medium pre-mix ~~which comprises an inhibitor or comprising a compound as defined in claim 27.~~

Claim 33 (original): A culture of cells in which the culture medium is as defined in claim 32.

Claim 34 (original): A culture according to claim 33 in which the cells are islet cells.

Claim 35 (currently amended): *Ex vivo* cells prepared by ~~a process the method~~ according to claim 22.

Claim 36 (currently amended): *Ex vivo* cells according to claim 35, wherein said cells are in a preparation ~~that comprises an inhibitor or comprising an inhibitor, wherein said inhibitor comprises a compound selected from the group consisting of~~

- (i) 3-(3-hydroxy-1-propyl)amino-1-propanesulfonic acid;
- (ii) DL-2-amino-5-phosphovaleric acid;
- (iii) 1,2,3,4-tetrahydroisoquinoline;
- (iv) cyclohexylsulfamic acid;
- (v) O-phospho-L-serine;

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- (vi) hexafluoroglutaric acid;
- (vii) 8-methoxyquinoline-5-sulfonic acid;
- (viii) 4-phenyl-1-(3'-sulfopropyl)-1,2,3,6-tetrahydropyridine;
- (ix) 3-amino-2-hydroxy-1-propanesulfonic acid; ~~or~~
- (x) 3-dimethylamino-1-propanesulfonic acid;
- ~~and pharmaceutically acceptable esters, acids, and salts or a salt thereof.~~

Claim 37 (previously cancelled).

Claim 38 (previously cancelled).

Claim 39 (previously cancelled).

Claim 40 (previously cancelled).

Claim 41 (previously amended): A pharmaceutical composition comprising a cell according to claim 35 and a pharmaceutically acceptable carrier or diluent.

Claim 42 (previously cancelled).

Claim 43 (currently amended): A vessel for containing a culture of cells, ~~which wherein~~ ~~said~~ vessel is coated with ~~an inhibitor or~~ a compound as defined in ~~claim 2~~ claim 27.

Claim 44 (previously amended): A kit for culturing cells comprising a culture medium or culture medium pre-mix as defined in claim 32.

Claim 45 (previously cancelled).

Claim 46 (currently amended): ~~Method~~ **A method** of identifying an inhibitor that can be used to prepare cells for transplantation in ~~a process~~ **the method** according to claim 22, comprising contacting a candidate substance with a mammalian cell and determining whether the candidate substance inhibits the formation of fibrils or causes the breakdown of fibrils, ~~(i) the inhibition of formation of fibrils or (ii) the breakdown of fibrils,~~ ~~indication~~ **indicating** that the substance is an inhibitor that can be used in said process.

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Claim 47 (previously amended): ~~Method A method~~ of identifying an inhibitor that can be used to prepare cells for transplantation in ~~a process the method~~ according to claim 22, comprising contacting a candidate substance with a protein capable of forming fibrils, or with a fibril, and determining whether the substance inhibits the formation of the protein into a fibril, or whether the substance causes the breakdown of ~~fibrils the fibril~~, (i) ~~inhibition of fibril formation or~~, (ii) ~~the breakdown of fibrils~~, indicating that the substance can be used in said process.

Claim 48 (previously cancelled).

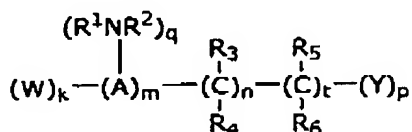
Claim 49 (previously cancelled).

Claim 50 (previously cancelled).

Claim 51 (previously cancelled).

Claim 52 (previously cancelled).

Claim 53 (new): The method according to claim 22, wherein said inhibitor comprises a compound according to the formula



wherein

k, m, t, p and q are independently 0 or 1;

n is an integer from 0 to 3;

C is a carbon;

N is a nitrogen;

W is hydrogen or an anionic group at physiological pH;

Y is an anionic group at physiological pH;

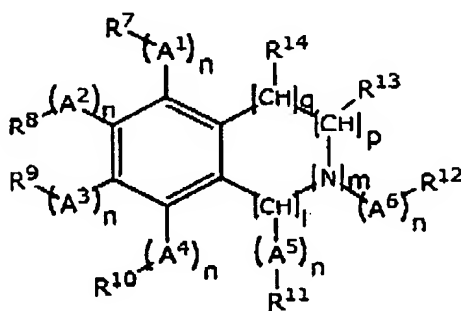
R¹ and R² are independently hydrogen, alkyl, an anionic group at physiological pH, or R¹ and R², taken together with the nitrogen to which they are attached, may form an unsubstituted or substituted heterocycl having from 3 to 7 atoms in the heterocyclic ring;

R³ hydrogen, halogen, thiol or hydroxyl;

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R^4 , R^5 , and R^6 are independently hydrogen or halogen; and
 A is hydrogen or C_1 to C_6 alkyl;
 and pharmaceutically acceptable esters, acids, and salts thereof.

Claim 54 (new): The method according to claim 22, wherein said inhibitor comprises a compound according to the formula



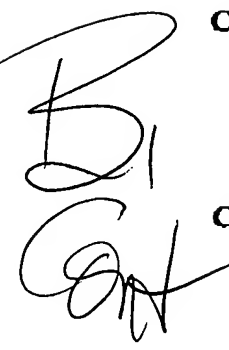
wherein

C is a carbon;
 N is a nitrogen;
 H is a hydrogen;
 A^1 , A^2 , A^3 , A^4 , A^5 and A^6 are independently alkyl, O, S, or -NH;
 m and n (for each individual A group) are independently 0 or 1;
 p, q and l are independently 0, 1, or 2;
 R^7 , R^8 , R^9 , R^{10} , R^{11} , R^{12} and each R^{14} are independently hydrogen, alkyl, alicyclyl, heterocyclyl or aryl, each R^{13} is independently hydrogen, alkyl, alicyclyl, heterocyclyl, aryl or an anionic group, and adjacent R groups may form an unsubstituted or substituted cyclic or heterocyclic ring;
 and pharmaceutically acceptable esters, acids, and salts thereof.

Claim 55 (new): The method according to claim 22, wherein the cells are islet, liver, muscle, kidney, neuronal, or stem cells.

Claim 56 (new): The method according to claim 22, wherein the cells are human, primate, rodent, rabbit, ovine, porcine, feline, or canine cells.

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**Claim 57 (new):** The method according to claim 22, wherein the amyloid deposits comprise islet amyloid polypeptide, A β peptide, prion protein, immunoglobulin light chain, amyloid A protein, transthyretin, cystatin, β 2-microglobulin, apolipoprotein A-1, gelsolin, calcitonin, atrial natriuretic factor, lysozyme variants, insulin, or fibrinogen.

Claim 58 (new): The method according to claim 22, wherein the cells are islet cells and the deposits comprise islet amyloid polypeptide.

["Remarks/Arguments" on following page.]